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NOVEL THERAPEUTIC MOLECULES

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FIELD OF THE INVENTION

- 5 The present invention relates generally to novel molecules capable of, *inter alia*,
modulating apoptosis in mammalian cells and to genetic sequences encoding same. More
particularly, the present invention relates to a novel member of the Bcl-2 family of
proteins, referred to herein as "Bim", and to genetic sequences encoding same. The
molecules of the present invention are useful, for example, in therapy, diagnosis, antibody
10 generation and as a screening tool for therapeutic agents capable of modulating
physiological cell death or survival and/or modulating cell cycle entry.

BACKGROUND OF THE INVENTION

- 15 Bibliographic details of the publications referred to by author in this specification are
collected at the end of the description. Sequence Identity Numbers (SEQ ID NOs.) for the
nucleotide and amino acid sequences referred to in the specification are defined following
the bibliography. A summary of the SEQ ID NOs. is provided before the Examples.
- 20 Apoptosis, the physiologic and genetically modulated process of cell death, is of central
importance for modelling tissues and maintaining homeostasis in multicellular organisms
(Kerr *et al.*, 1972; Jacobson *et al.*, 1997). Great progress is being made towards
understanding the biochemistry underlying this intrinsic suicide program. The cellular
apoptotic effector molecules include a set of cysteine proteinases, termed caspases, that
25 degrade critical cellular substrates (Nicholson and Thornberry, 1997). The regulatory
machinery that governs the activation of the caspases is less well understood. However a
family of proteins of which Bcl-2 is the prototypic molecule (and is referred to as the Bcl-
2 family of proteins) plays a central role (Jacobson, 1997; Reed, 1997; Kroemer, 1997).
- 30 Bcl-2 was the first intracellular regulator of apoptosis to be identified (Vaux *et al.*, 1988)
and high levels enhance cell survival under diverse cytotoxic conditions. Other cellular